REMARKS

Applicants have canceled calms 85-89, 91, 92, and 95-99 without prejudice or disclaimer. Claims 90, 93, and 94 are currently pending.

Claim 90 is amended for clarity and to include certain elements from previously presented claims 91 and 92. Support for claim 90 as amended can be found throughout the specification as filed, for example, at pages 50-51. Claims 93 and 94 have been amended for clarity and to update their dependency. Support for claims 93 and 94 as amended can be found throughout the specification, for example at pages 50-51. As such, no new matter has been added by way of this amendment.

Without acquiescing to the rejections of the Office Action mailed October 2, 2006 (Office Action) and solely to expedited prosecution, Applicants have canceled claims 85-89, 91, 92, and 95-99. Accordingly, Applicants will not address the rejections as to those canceled claims.

Reconsideration of the pending claims in view of the amendment and remarks presented herein is respectfully requested.

Rejection of claims 90, 93, and 94 under 35 U.S.C. § 112, first paragraph (written description)

The Examiner rejected claims 90, 93, and 94 under 35 U.S.C. § 112, first paragraph as allegedly containing subject matter that was not described in the specification in such a way as to reasonably convey to a skilled artisan that the inventors had possession of the claimed subject matter at the time of filing the application. See Office Action at page 2.

The test for sufficiency under the written description requirement of 35 U.S.C. §112, first paragraph is found in Vas-Cath, Inc. v. Mahurkar, 935 F.2d 1555, 19 U.S.P.Q.2d 1111 (Fed. Cir. 1991). In that case, the Federal Circuit remarked that although the applicant "does not have to describe exactly the subject matter claimed . . . the description must clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed" (citations omitted). The Examiner bears the initial burden of establishing that the claims are unpatentable for want of written description. See MPEP 2163.04 and In re Marzocchi, 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA 1971) ("The description as filed is presumed to be adequate, unless or until sufficient evidence or reasoning to the contrary has been presented by the examiner to rebut the presumption"). In the instant case, the Examiner has not met this initial burden of showing why a person skilled in the art would not recognize that the applicant was in possession of the invention as claimed.

The Examiner asserted that "[n]o common structural attributes identify the members of the claimed genus, and distinguish members within the claimed genus form those outside of the claimed genus." Office Action at page 3. Applicants respectfully disagree. Claim 90, as amended, recites methods using a single-stranded oligoribonucleotide 12 to 30 nucleobases in length, wherein said single-stranded antisense oligoribonucleotide comprises: (i) no more than two mismatched nucleobases relative to said target messenger RNA, (ii) a 2'-fluoro modification at each nucleoside of said single-stranded antisense oligoribonucleotide, (iii) a 5' terminal phosphate, and (iv) at least one phospohorothioate linkage. Those elements describe structural attributes that do distinguish the claimed methods and demonstrate possession of such methods by the inventors at the time of filing.

The Examiner also asserts that "the specification and claims do not adequately teach a representative number of species for the broad genus claimed." Office Action at page 3. However, it is well settled that working examples are not required to satisfy the written description requirement. For example in Falkner v. Inglis, No. 05-1324 (US Court of Appeals for the Federal Circuit, May 26, 2006) the Federal Circuit concluded that:

> (1) examples are not necessary to support the adequacy of a written description (2) the written description standard may be met (as it is here) even where actual reduction to practice of an invention is absent; and (3) there is no per se rule that an adequate written description of an invention that involves a biological macromolecule must contain a recitation of the known structure.

The decision by the Federal Circuit in Falkner is in accordance with prior case law, including Lizard Tech, Inc. v. Earth Resource Mapping, PTY, Inc. 424 F.3d 1336, 1345 (Fed. Cir. 2005) and Union Oil Co. v. Atlantic Richfield Co. 208 F.3d 989, 997 (Fed. Cir. 2000), which concluded, "A claim will not be invalidated on section 112 grounds simply because the embodiments of the specification do not contain examples explicitly covering the full scope of the claim language."

Thus, the written description requirement does not necessitate an exhaustive listing of every embodiment that falls within the scope of the claims when a generic description is provided. Applicants have not only supplied such generic description (see e.g., pages 5-6, 41-44), but have provided a specific example of the claimed methods. See Example 13, at page 50-53. That example, together with the specification, including the claims as originally filed (see e.g., original claim 56 and

claims depending therefrom) clearly demonstrate to one of skill in the art that the inventors were in possession of the claimed invention at the time the application was filed.

Applicants respectfully submit that for at least these reasons, the Examiner has failed to establish that one of ordinary skill in the art would not reasonably believe that Applicants were in possession of the claimed invention. Accordingly, Applicants respectfully requests withdrawal of the rejection under 35 U.S.C. §112, first paragraph. Claims 85-89, 91, 92, and 95-99 have been canceled. Thus, the rejection of those claims is moot.

Rejection of claims 90, 93, and 94 under 35 U.S.C. § 112, first paragraph (enablement)

The Examiner rejected claims 90, 93, and 94 under 35 U.S.C. § 112, first paragraph as allegedly not being enabled by the specification. Applicants respectfully disagree.

An application enables the claims "if one skilled in the art, after reading the disclosure, could practice the invention claimed . . . without undue experimentation." Chiron Corp. v. Genentech, Inc., 363 F.3d 1247, 1253 (Fed. Cir. 2004). "But the question of undue experimentation is a matter of degree. The fact that some experimentation is necessary does not preclude enablement; what is required is that the amount of experimentation 'must not be unduly extensive.'" PPG Indus., Inc. v. Guardian Indus., Corp., 75 F.3d 1558, 1564 (Fed. Cir. 1996) (quoting Atlas Powder Co. v. E.I. DuPont de Nemours & Co., 750 F.2d 1569, 1576 (Fed. Cir. 1984)).

The Examiner asserts that the specification does not enable "methods of eliciting cleavage of any target mRNA." Office Action at page 4. However, the specification provides guidance in targeting (e.g., pages 16-17) and screening (e.g., pages 41-44). Such strategies may be employed by one of ordinary skill to identify target messenger RNA the cleavage of which may be elicited according to the claimed methods. The question is whether doing so constitutes "undue experimentation" as asserted by the Examiner. It is well established that undue experimentation is not measured by the amount of time, expense or quantity of experimentation that is involved in implementing the disclosed methods. See In re Wands 858 F.2d 731 (Fed. Cir. 1988); United States v. Telectronics Inc., 857 F.2d 778 (Fed. Cir. 1998); and M.P.E.P. § 2164.06. Provided that the procedure used to implement the claimed invention is routine, it is of little consequence to enablement the number of iterations or the length of the procedure that is required before the end is achieved. In view of the specification and the prior art of record, the skilled artisan has a clear path to practice the claimed invention.

Indeed, Applicants note that in the context of a § 103 rejection, the Examiner remarked that targeting particular sequences and incorporating chemical modifications in the oligribonucleotide would require only "routine screening." See Office Action at page 10 and at page 11 ("Elbashir provides a rational approach to the routine optimization of siRNA molecules for eliciting target mRNA cleavage, including the testing of incorporation of routine oligonucleotide modifications . . . McKay et al also teaches the in vitro inhibition and routine screening of modulators comprising various configurations of modifications for their ability to target and inhibit expression of mRNA in vitro . . . the incorporation of various modifications including incorporation of 2'-O or 2'-Fluoro modifications, phophorothioates, enhance oligonucleotide stability target cell uptake and target binding and the particular configuration would require routine screening as taught previously . . . enhanced cleavage of target genes in vitro and to test for optimal configurations would be routine experimentation to one of ordinary skill in the art.").

Applicants respectfully submit that the specification provides sufficient guidance to enable one of ordinary skill in the art to fully practice the claimed invention requiring only routine experimentation. Thus, Applicants respectfully request that the Examiner withdraw the rejection of claims 90, 93, and 94 under 35 U.S.C. § 112, first paragraph as related to enablement. Claims 85-89, 91, 92, and 95-99 have been canceled. Accordingly, the rejection of those claims is moot.

Rejection of claims 90, 93, and 94 under 35 U.S.C. § 103(a)

The Examiner rejected claims 90, 93, and 94 as allegedly obvious under 35 U.S.C. § 103(a). In particular, the Examiner asserted that claims 90, 93, and 94 are "unpatentable over Fire and Zamore et al. and Elbasher et al., in view of McKay." Office Action at page 9.

To establish a prima facie case of obviousness a three-prong test must be met. First the prior art must teach or suggest all the claim limitations; second, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available among those of ordinary skill in the art, to combine or modify the reference(s); and third, there must e a reasonable expectation of success. See In re Vaeck, 947 F.2d 488 (Fed. Cir. 1991).

Applicants respectfully submit that claims 90, 93, and 94 are not obvious. For the sake of clarity, claim 90 has been amended to recite "single-stranded." Since Fire et al., Zamore et al., and Elbashir et al., describe double-stranded RNA complexes, Applicants respectfully submit that they do

not render obvious the present claims. Indeed, these references teach away from methods using single-stranded oligoribonucleotides. See e.g., Fire et al., at Col 3 (remarking that "dsRNA is at least 100-fold more effective than the injection of purified antisense [single-stranded] RNA"). Accordingly, application of these references to the present claims is inapt.

McKay et al., does not teach or suggest every element of the claims. For example, McKay et al. does not disclose an oligoribonucleotide comprising a 2'-fluoro modification at each nucleoside, at least one phophorothioate, and a 5' terminal phosphate. For at least that reason, McKay et al. does not render the present claims obvious.

In view of the foregoing remarks, Applicants respectfully request that the Examiner withdraw the rejection of claims 90, 93, and 94 as obvious under 35 U.S.C. § 103(a). Claims 85-89, 91, 92, and 95-99 have been canceled. As such, the rejection with respect to those claims is moot.

CONCLUSION

Applicants believe that all outstanding issues in this case have been resolved and that the present claims are in condition for allowance. Nevertheless, if any undeveloped issues remain or if any issues require clarification, the Examiner is invited to contact the undersigned at the telephone number provided below in order to expedite the resolution of such issues.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 50-0252.

Respectfully submitted,

Dated: 4/2/07

By: 

Clifford E. Ford
Registration No. 52,903
Isis Pharmaceuticals, Inc.
760-603-2784